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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,166	03/01/2004	Israel R. Charo	02307K-085041US	3893

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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 11/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/791,166	CHARO ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7,9,10,13,16 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7,9-10,13,16,18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments and remarks filed 29 September 2005 have been entered. Claims 2-3, 5-6, 8, 11-12, 14-15, and 17 are canceled; claim 18 is new. Claims 1, 4, 7, 9 – 10, 13, 16 and 18 are pending and under examination.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Withdrawn Objections and Rejections

4. The following objections and rejections made in the previous office action are withdrawn in light of applicant's amendments.

1) The objections to the specification.

2) The objections to the claims; applicant has canceled the offending claims.

3) The rejection under 35 USC 112, first paragraph, for lacking adequate written description; applicant has canceled the offending language.

4) The rejection under 35 USC 112, second paragraph. Applicant has canceled the offending language.

Maintained Rejections and Objections

Priority

5. The examiner notes that the specification appears to be identical to some the previously-filed specifications. Applicant argues, on p. 8 of the remarks, that he is entitled to an effective filing date of 13 January 1994, the date 08/182,962 was filed. However, several elements are now claimed which do not find support in either the specifications or claims of the parent applications. The first appearance of a method of inhibiting a condition characterized by monocytic infiltrates comprising administering an antibody to MCP-1 receptor appears in claim 1 of the instant application as originally filed. There is not explicit disclosure or contemplation of methods of administering antibodies for treatment of disease or condition in any of the previous applications. The examiner notes that p. 26, lines 18 – 27 of application 08/182962 provide support for administration of *MCP-1 receptor antagonists* for treatment of disease, but *MCP-1 receptor antagonists are not the same as antibodies.* According to the '962 specification and to

the specifications of all other applications from which the instant application claims priority, antagonists are structurally undefined and are to be identified by performing screening assays. Therefore the filing date for the claims drawn to methods of treating disease by administering antibodies receive benefit of the date that such activity was first contemplated, namely 1 March 2004, the date the instant application was filed.

Should applicant continue to disagree with the examiner's factual determination, it is incumbent upon applicant to provide evidence demonstrating that the previously-filed applications do in fact contemplate administration of antibodies for treatment of disease. This could be accomplished, for example, by pointing out the specific page and line numbers of the previously filed applications where there is support for the concept of administering antibodies for treatment of disease.

Claim Rejections - 35 USC § 112

6. Claims 1, 4, 7, 9 – 10, 13, 16 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administration of anti-MPC-1 receptor antibodies, does not reasonably provide enablement for inhibition of any condition characterized by monocytic infiltrates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is maintained for the reasons made of record in the previous office action and extended to new claim 18 as well.

Applicant argues, on p. 9 of the remarks, that a considerable amount of experimentation would not be considered undue if such experimentation is routine in the field. The examiner concedes that since the prior art publication by Monteclaro et al. (1997. Journal of Biological Chemistry 272:23186-23190, cited in previous office action) discloses which regions of the receptor are necessary and sufficient for binding to MCP-1, the amount of experimentation required to make an antibody which binds to SEQ ID NO:2 or 4 and inhibits the activity would not be undue.

Applicant argues, on p. 11 of the remarks, that there is sufficient guidance to which antibodies can be used in the method. In light of the amendments to claim 1, the examiner concedes this point.

Applicant argues, on p. 12, that paragraph 0028 provides support for adequate enablement of conditions characterized by monocytic infiltrates. The examiner notes that the

enclosed article by Gu et al. (J Leukoc Biol. 1997 Nov;62(5):577-80), which was published seven years prior to the effective filing date of this application, indicates those conditions which are characterized by monocytic infiltrates and thus concedes this point as well.

On p. 13, applicant argues that there is adequate support for the limitation "therapeutically effective amount", which appears in claim 10. The quotation provided by applicant fro *Angstadt* is particularly relevant. The instant specification does not provide any working examples of administration of antibodies to patients, at any concentration. There are not even working examples of antibodies administered to animal models, or to cell cultures *in vitro*. While the specification does state that the effective dose is in the range of about 10 ug to about 1 mg per ml per dose administered, this is a very broad range, encompassing at least two orders of magnitude. Furthermore, since the units are recited as "per milliliter per dose administered", and there is no guidance as to how many ml are to be administered, it is actually not guidance as to the dose, but rather the concentration. The specification clearly does not provide adequate guidance for the skilled artisan to be able to administer a therapeutically effective amount. The artisan would essentially have to engage in trial-and-error experimentation, which would be undue.

7. Claims 1, 4, 7, 9 – 10, 13, 16 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

This rejection is maintained for the reasons made of record in the previous office action and reiterated herein. The rejection also applies to new claim 18.

Applicant argues that there is support for "binding fragment thereof" but such language has been canceled. The examiner concedes that the term "about 10 ug / ml to about 1 ug/ml" appears in the instant application, and in 08/446669, and in 08/182962 (see p. 27 lines 8 – 9 for example). However, the recitation of this term in all applications is drawn to the effective amount of the uncharacterized antagonist, which is to be identified by a screening assay. Mere recitation of the term does not constitute adequate support for the administration of antibodies at this concentration.

Applicant argues that paragraph 0015 provides adequate support for the term "monoclonal antibody". The examiner disagrees. The term does not appear in the cited

paragraph, or anywhere in the specification. Applicant also argues that citation of several textbooks and laboratory manuals, along with the statement that they are incorporated by reference, provides sufficient support for the term. Applicant is directed to MPEP § 608.01(p)(I)(A), particularly the third paragraph which states:

> "Mere reference to another application, patent, or publication *is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph.* In re de Seversky, 474 F.2d 671, 177 USPQ 144 (CCPA 1973). In addition to other requirements for an application, the referencing application should include an identification of the referenced patent, application, or publication. *Particular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found.*" (emphasis added)

Clearly the specification does not point the artisan to any particular passages in the texts. Therefore there is not sufficient support for the term "monoclonal antibody". Furthermore there is not support for Fab fragments, recited in new claim 18, so claim 18 is also rejected for containing new matter.

As stated in more detail in the section entitled "priority" above, there was *no contemplation* of administration of antibodies prior to the filing of the instant application. Therefore, all recitations of administration of antibodies are considered new matter.

Claim Rejections - 35 USC §§ 102 and 103

8. Claims 1, 7, 9 – 10, 13, 16, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by LaRosa et al. (U.S. Patent 6,312,689, cited by applicant on IDS filed 20 May 2005). This rejection is maintained for the reasons made of record in the previous office action. Applicant argues that the effective filing date of the instant application is 11 January 1995. However as explained in the section entitled "priority" above, there was *no contemplation* of administration of antibodies prior to the filing of the instant application. Therefore the effective filing date is the date the instant application was filed, specifically 1 March 2004. LaRosa's methods include administration of Fab fragments, as these are explicitly recited at column 9, lines 52 – 60, thereby anticipating new claim 18.

9. Claims 4 and 13 are rejected under 35 U.S.C. 103(a) as obvious over LaRosa et al. for the reasons made of record in the previous office action. Applicant argues that the effective

filing date of the instant application is 11 January 1995. However as explained in the section entitled "priority" above, there was *no contemplation* of administration of antibodies prior to the filing of the instant application. Therefore the effective filing date is the date the instant application was filed, specifically 1 March 2004.

Rejections Necessitated by Amendment

10. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is drawn to an antibody which is a Fab fragment. However a fragment is not an antibody; it is a fragment of an antibody.

Conclusion

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.
November 9, 2005

SHARON TURNER, PH.D.
PRIMARY EXAMINER
11-16-05